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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,044	08/03/2001	Plamen A. Demirev	UMARY 5	4090

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
KENEDY, ANDREW A	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 05/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/856,044	DEMIREV ET AL.	
	Examiner	Art Unit	
	Andrew A. Kenedy	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Cancellation of Claim 6 and amendment of Claim 1 in Applicants' preliminary amendment received June 18, 2001, is acknowledged. Claims 1-5 and 7-11 are currently pending.

Claim Rejections - 35 USC § 112

Claims 1-5 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the particular microorganisms *E.coli* and *B.subtilis*, does not reasonably provide enablement for other bacteria such as *Haemophilus influenzae, Streptococcus pneumoniae, Streptococcus pyogenes, Clostridium tetani, Mycobacterium tuberculosis, Bordetella pertussis,* or viruses, or mammalian tumor cells , etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Wang et al. (*Rapid Communications in Mass Spectrometry*, 1998), relied upon in the art rejections below, explains that the primary challenge (and key to successful implementation) in using mass spectral analysis of crude bacterial preparations is to have a previously established subset of peptides/proteins (whose mass spectrum peaks are characterized) to use in differentiating between different species of bacteria, which in the case of the bacterium *E.coli* for example, have over 4000 individual proteins, many of which overlap with protein mass peaks in mass spectrum of other species of bacteria (see at least pg. 456, col. 1, paragraph 1; and pg. 459, col. 1, bridge paragraph). Wang et al. explains that one must identify which of these particular peptide/protein masses have validity as 'biomarkers' for discrimination between the different bacteria (see at least pg. 456 col. 2, paragraph 1 – pg. 457, col. 1, bridge paragraph). Wang et al.

further explains that this depends on a number of experimental factors that can vary between methods used by different laboratories, namely protein extraction methods and sample/matrix preparation techniques which -- because of differences in extraction solvents, pH of extraction solutions, and salt content of sample preparations -- "can have a major impact on observed spectra" (see at least pg. 463, col. 1 – col. 2). In the absence of a disclosure of valid peptide/protein biomarkers for all microorganisms encompassed by the instant claims, or alternatively providing guidance in the form of methods by which to circumvent this need, Applicants appear to have failed to provide enablement of their invention for any microorganisms other than *E.coli* and *B.subtilis*. It would require undue experimentation for one of ordinary skill in the art to use Applicants' instant invention for differentiation between other species of microorganisms for the above reasons.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 and 7-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (*Rapid Communications in Mass Spectrometry*, 1998), in view of Yates, III et al. (US 5538897 A).

Regarding Claim 1, Wang et al. teaches a method of identifying bacteria using mass spectrometry comprising: searching a sequence database for a plurality of proteins that are

predicted to have the same masses (molecular weights) as proteins in the mass spectrum of a sample, whereby unknown microorganisms are identified. Wang et al. further teaches that the sample comprises a plurality of proteins from one or more unknown microorganisms, and said database is searched for more than one different protein (see at least pg. 456 all; pg. 463, col. 2, paragraph 4; and pg. 459, col. 1, bridge paragraph).

Regarding Claims 2 and 3, Wang et al. teaches that the mass spectral patterns should be used to identify and search for protein biomarkers via their observed masses, rather than relying on spectral pattern differences such as differences in spectral peak magnitudes, and that an 'integrated approach' using these protein masses can involve a peptide database (the sequence database can be a protein sequence database) or relating the protein masses to gene sequences that code for their production (the sequence database is a nucleotide sequence database) (see pg. 463, col. 2, paragraph 4; and pg. 459, col. 1, bridge paragraph).

Regarding Claim 4, Wang et al. teaches that the mass spectrometry data is MALDI-TOF data (see at least the abstract).

Regarding Claim 5, Wang et al. teaches that the mass spectrometry data is obtained by electrospray on a time-of-flight mass analyzer (see at least pg. 456, col. 1, paragraph 2 – col. 2, bridge paragraph).

Regarding Claim 7, Wang et al. teaches that the method comprises performing a mass spectral analysis on a sample comprising one or more microorganisms (see at least Fig. 1-9; and col. 1, paragraph 1).

Regarding Claim 8, Wang et al. teaches that the method further comprises identifying masses (molecular weights) of proteins in a mass spectrum of said sample (see at least pg. 457, col. 1, bridge paragraph; and pg. 459, col. 1, bridge paragraph).

Regarding Claim 9, Wang et al. teaches that one goal is to be able to identify and differentiate between different species of bacteria cells present in 'real world samples' (the sample comprises at least two different species of microorganisms) (see at least pg. 456, col. 1, paragraph 1).

Wang et al. does not explicitly teach that the database is searched for intact, undigested proteins as in Claim 1; that the sequence database can be the NCBI/SwissProt/EMBL database as in Claim 10; or that the method can comprise chemical or enzymatic digestion of a protein in said sample as in Claim 11.

Yates III et al. teaches a method for using sequence databases to identify amino acid sequences of protein spectrum obtained by mass spectrometry wherein the database is searched for intact, undigested proteins as in Claim 1 (see at least col. 4, lines 14-24 and lines 49-65); that the sequence database can be the GenBank, SWISS-PROT, or EMBL database (the NCBI/SwissProt/EMBL database) as in Claim 10 (see col. 3, lines 53-67); or that the method can comprise trypsin enzymatic digestion of a protein sample as in Claim 11 (see at least col. 10, lines 43-48).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Yates III et al. with the methods of Wang et al., since Yates III et al. and Wang et al. both teach methods for identifying proteins in a sample by using mass spectrometry results to search peptide/protein databases (see above) and since Yates III et al. teaches that "it would be useful to

provide a system for correlating fragment spectra with known protein sequences while avoiding the delay and/or subjectivity involved in hypothesizing or deducing candidate amino acid sequences from the fragment spectra. According to the present invention, known amino acid sequences, e.g., in a protein sequence library, are used to calculate or predict one or more candidate fragment spectra." (see col. 1, lines 58-67).

Made of Record

Prior art of record that discloses aspects of Applicants' instant invention but not relied upon: Claydon et al. (Applicants' IDS document No. 12) which teaches MALDI-TOF spectrometry for the identification of genus/species of microorganisms in samples by comparison of spectral data to a database; Pineda et al. (Applicants' IDS document No. 14) which teaches MALDI-TOF spectrometry for the identification of microorganisms by comparison of spectral data to Internet-accessible proteomic databases; Krishnamurthy et al. (Applicants' IDS document No. 18) which teaches MALDI spectrometry for rapid identification of bacterial whole cells in environmental samples; van Adrichem et al. (Applicants' IDS document No. 22) which teaches MALDI spectrometry for characterizing protein profiles in mammalian cells.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew A. Kenedy whose telephone number is (571)-272-0574. The examiner can normally be reached on Monday-Friday 9:00am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.A.K. May 10, 2004

Marianne P. Allen 5/11/04
MARIANNE P. ALLEN
PRIMARY EXAMINER
AU1631